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Cognitive and Neural Bases of Skilled Performance

A UNIVERSITY RESEARCH INITIATIVE

by Lloyd Kaufman and Samuel J. Williamson
Principal Investigators

New York University

Prepared for:

Dr. A.R. Fregly
Directorate of Life Sciences
Air Force Office of Scientific Research
Bolling AFB, DC 20332

Approved by:

Lloyd Kaufman
Lloyd Kaufman

Samuel J. Williamson
Samuel J. Williamson

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Major improvements were introduced for neuromagnetic studies by the installation of a magnetically shielded room and versatile gantry to hold our 5-sensor neuromagnetometer. Studies with this system verify that the strength of the 100-ms component of the cortical response to a tone is unaffected by tone frequency and intensity at suprathreshold levels, but we have shown that both the 100-ms and 180-ms components are affected by attention. Moreover, we have obtained evidence that auditory cortex in left and right hemispheres may have differing responses to a tone depending on the inter-stimulus interval. Neuronal sources of certain components of auditory-evoked responses are found to be displaced across cortex from the others, with a tonotopic representation for the 50-ms transient component apparently differing from the representation for the steady-state component, which has a similar apparent latency. Studies of spatial attention have revealed robust effects for latencies exceeding 200 ms, unlike for the auditory system, but some subjects show effects commencing as early as 100 ms. The corresponding attention operating characteristics were determined in psychophysical studies. An investigation of the classic P300 response for both visual and auditory stimulation has been initiated with a more efficient paradigm, and early results provide evidence that the neuronal

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source is independent of sensory modality. To address the question of how much cortex is involved in producing an evoked field or potential, we have analyzed published data on intracortical voltage measurements in cat and monkey and found that the current dipole moment per square millimeter of cortical area is very much the same at moments of peak activity for long-latency responses. From this we deduce that the area in human cortex typically ranges from 40 to 400 mm^2, based on the current dipole moments deduced from neuromagnetic data. Several significant technical developments were made during this period. They include: a device for indexing positions on the scalp so that pixels in magnetic resonance images can be accurately specified by 3-D coordinates referenced to landmarks on the subject's scalp; a method for locating a small magnetic object within the human body, with verification by surgery; a method for calibrating multisensor SQUID systems; and a procedure for locating a neuronal source in human sensory cortex with a reproducible accuracy of better than 3 mm.

Table of Contents

This report, which is submitted in accord with the requirements of Contract No. F49620-88-C-0131 between AFOSR and New York University, describes the scientific progress made in the final year and summarizes the accomplishments over the entire term of the project.

The original proposed project, which began in September, 1986, had four basic components. These included the improvement of university facilities to permit the conduct of advanced research that would be in the interest of the Department of Defense, the actual conduct of such research, the training of students and postdoctoral personnel to conduct the research, and the coordination of research and training efforts with Department of Defense laboratories which would be to the mutual benefit of the University and the DoD. This Technical Report describes our progress to date in the scientific areas.

One of the goals of this project was to enhance the instrumentation and technology involved in measuring and analyzing the brain's magnetic field so that it would become possible to study brain activity related to various aspects of human performance. A special emphasis was placed on the way in which workload affects the activity of the brain and, *ipso facto*, the performance of the human operator. An equally important goal was the design and conduct of meaningful substantive experiments concerning aspects of brain activity underlying processes such as attention and its deployment in various tasks. The following section reviews our accomplishments in all of these areas over the term of the project.

Overview

The performance of a complex task, like piloting an aircraft or diagnosing the cause of a malfunction in a complex system, depends strongly upon cognitive skills. Our knowledge of the mechanisms of cognition (which includes attention, memory, learning, decision making and perception) is very limited, and this constrains our ability to assess and predict performances in complex tasks. The aim of our program was to contribute to this basic knowledge by encouraging prominent researchers in these areas to find common foci so that their efforts mutually reinforce each other. One focus that transcends the traditional boundaries of the individual disciplines comprising *cognitive science* is that of the role of the human brain.

Our understanding of the activity of the brain and how it relates to cognition and performance is sharply limited by the brain's complexity as well as by its inaccessability. Any means for improving access to the brain's activity and for discovering the relation of this activity to cognition is bound to be of interest to a multidisciplinary group of researchers and their students.

Studies of the brain should clarify the nature of otherwise unobservable processes that underly performance. Without this, cognitive science is left with untestable theories of underlying mechanisms. The field abounds with examples of ongoing arguments. For example, does the machinery of the visual system involved in the perception of real objects play a role in the formation and processing of mental images? This question is of concern to many authors, but recent advances in the neurosciences are making it possible to arrive at an objective answer to the question. As to the relevance of the question, it is worth noting the evidence indicating that the ability to "visualize" situations has an effect on objective measures of certain perceptual-motor tasks. Perhaps more important are the implications of a role for sensory cortex in mental imagery. If such a role is confirmed it would imply that sensory, and possibly motor areas of neocortex are actively involved in the

processes of short-term active memory. As we shall see, this was actually one ultimate outcome of our project.

The technological advances in the field of neuromagnetism contributed to this result. As a result of three years of work in the URI program we have learned much about how to integrate research activities in the fields of cognitive psychology, perception, and neuromagnetism. This final report describes the major developments resulting from the program and gives some idea of how it affected recent work at NYU. Earlier annual technical reports dealt in detail with other areas supported by the URI, but owing to funding reductions work on those areas was suspended prior to the last Interim Technical Report, so it shall not be repeated here.

A Role for Neuromagnetism

In general, new methods for the study of brain activity represent remarkable advances over those available just a few years ago. Technologies attracting the greatest interest are those that identify the anatomical sites of activity so their specific functions can be elucidated. The earliest development occurred in two techniques that measure physiological processes accompanying neuronal activity. Single photon emission tomography (SPECT) and positron emission tomography (PET) are the best known, and measurements of photon distributions from appropriate radioactive tracers introduced into the blood provide measures of local blood flow rate and glucose metabolism. The application of these techniques to cognitive processes is limited by considerations of sensitivity (photon counts). Consequently, data must be recorded over a relatively long period of time to attain a significant reading. There may well as well be inherent limitations in the time resolution when monitoring rapid activity, since membrane time constants are much shorter than changes in blood flow rates and metabolism. Moreover, to achieve the higher sensitivity required to register activity over shorter integration periods, materials with higher radioactive decay rates would be needed. Correspondingly, these materials must have shorter half-lives to respect exposure limits for human subjects. Use of ^{15}O with a half life of 2 minutes is one example. Such a short half life, on the other hand, limits the kinds of cognitive studies that can be carried out and verified on an individual subject. For such reasons, it is often necessary to average data over subjects to reveal the distribution of brain activity and how it varies with the nature of the cognitive task.

More recently, interest has developed in complementary techniques that provide a more specific and rapid measure of neuronal activity, *viz.* magnetic measurements of intracellular electrical current and electrical measurements of the accompanying volume current. Despite earlier dissappointments, increasingly sophisticated EEG techniques are making it possible to examine how activity shifts from one area to another during different types of performances and when correct and incorrect decisions are being made (Gevins et al., 1987). *** In addition, steady progress is being made in the study of attention using the event related potential of the EEG. We do not have the time to go into these related new technologies here, but shall briefly describe the complementary methods employed in the URI program at New York University.

The flow of ionic currents in the neurons of the brain gives rise to magnetic fields that can be detected outside the scalp. The main advantage in studying these fields, especially components of the field oriented radially with respect to the scalp, is that the intervening tissues are transparent to them, and they are largely undistorted by the changes in conductivity normally present within the skull. This makes it possible to locate sources with a precision and reliability of better than 3 mm in three dimensions. This claim is based on

theory (cf. Williamson and Kaufman, 1987) and has recently received experimental verification in a study funded in part by the URI (Yamamoto et al., 1988). During the course of the present program, considerable effort went into the development and refinement of the instrumentation (including superconducting sensors), installing and evaluating a magnetically shielded room, developing and procuring analytical hardware and software, and devising experimental procedures that are uniquely suited to this new technology. As a result, there have been many substantive research accomplishments.

Available Instrumentation

The Neuromagnetism Laboratory (NML) at NYU contains a 5-channel system that measures the field at five places at once outside the scalp. This is the main instrument used in the URI program, and is the prototype of all such instruments manufactured in the United States. However, NML also has access to a system composed of two 7-channel instruments which is located at the NYU Medical Center. The 5-channel system served as the model for the design and construction of these 7-channel systems. Although this twin 7-channel system was not funded by AFOSR, it was used in some of the studies connected with the URI, and some of the expenses incurred in its operation were covered by the existing URI project.

Experimental Studies

Auditory Attention

During the term of this project we completed a major study of selective auditory attention which was fully described in previous reports (See Curtis et al., 1988). In this study we employed a dichotic listening paradigm in which subjects attended to strings of tone bursts presented to one ear while ignoring similar bursts of different (more than an octave away in pitch) that were presented to the other ear. The significance of this paradigm for theories of attention is traced by Treisman (1964; 1967; 1969) with a typical opposing view by Deutsch and Deutsch (1963). (Also see Broadbent, 1957; 1958; and Cherry, 1953.) Responses evoked by both the ignored and attended signals contain components corresponding to the N100 component of the auditory event related potential (ERP). It was found that the N100m (the magnetic counterpart to the N100 of the ERP) varied in amplitude with attention, i.e., its amplitude was greater if attention was being paid to the stimulus. A similar effect was studied in detail by Hillyard and his colleagues with electrical recordings (Hillyard, et al., 1973; 1983; 1984; 1985). The latter papers dealt largely with the effect of attention on the amplitude of the N100 component of the ERP.

We went further than this by dealing with the problem of locating the equivalent current dipole source of the observed N100m, to determine whether attentional effects are exhibited by activity in primary auditory cortex. Moreover, by determining where neuronal activity takes place it is also possible to deduce a quantitative measure for this activity. In this way was possible to show that the attentional modulation of magnetic field is due to modulations of activity of a given neuronal population, rather than a large spatial shift of activity from one population to another. Neuromagnetic measurements show that the equivalent current-dipole source of the observed field of N100m is located in the cortical layer forming the floor of the Sylvian fissure in Herschl's gyrus (Yamamoto et al., 1988). These results demonstrated that activity of auditory cortex is modulated by attention. This conclusion should be contrasted with the previously widespread and prevailing view that the effect of selective attention on N100 could well be due to the summation of

endogenous activity of sources distant from auditory cortex with that of exogenous activity of a source or sources in auditory cortex (see Naatanen and Picton, 1987 for a review). In view of the fact that 30 - 50% changes in source strength (current dipole moment) was attributable to attention, and that the changes in ERP amplitudes are not larger than this, we must conclude that the modulation of auditory cortical activity plays a major role in the effect of attention on N100 of the ERP. Essentially the same results were found for conditions in which the subject's attention was allocated to stimuli that different in apparent direction (lateralization), or when the stimuli were presented to one ear and attention was allocated on the basis of a difference in pitch. No significant hemispheric conditions were observed. Despite this, there remains the possibility that other non-auditory cortical sources may contribute to the effect of attention on N100 detected electrically.

Although our data support a strong contribution of sources in auditory cortex to attention-related variations in N100, this does not rule out possible roles for other sources. In a spherical model radial current dipole sources make no contribution to the external magnetic field. Therefore, sources that are oriented radially with respect to the local contours of the overlying skull may be expected to make little contribution to the neuromagnetic field associated with N100m. However, these same "quasi-radial" sources would contribute strongly to the electrical N100.

Hemispheric Asymmetry and the Auditory Response

One of the stronger pieces of evidence that such magnetically weak or silent sources may contribute to N100 is the finding (Hari et al., 1982) that the amplitude of the electrical N100 increases monotonically with ISI up to ISIs as great as 16 seconds, while the N100m does not exhibit the same effect. This effect of ISI on N100 is quite striking, and it is reminiscent of the psychological refractory period studied by Karlin and Kestenbaum (1968). However, since the amplitude of N100m increased with ISIs only up to 8 seconds, it was concluded that additional and magnetically silent sources contributed to N100. These are presumably responsible for the increase in amplitude with ISI longer than 8 seconds. These sources are not necessarily located in auditory cortex.

In the course of our work on this project we noted that Hari et al. measured the field associated with N100m over only one hemisphere, while the vertex electrode used to detect N100 was sensitive to activity in both hemipsheres. It was postulated that asymmetrical variations in amplitude of N100 with ISI between the hemispheres could account for the discrepancy between the electrical and magnetic recordings.

As a follow-up to this early observation, we explored the possibility that variation in amplitude of N100m with ISI is asymmetrical, in that the sources of this component in each hemisphere show different effects of ISI. In March of 1987 a pilot study was conducted in collaboration with R. Hari. Using the same instruments and experimental paradigm as employed in the original study by Hari et al., it was found that the two hemispheres can show different effects of ISI. This was then replicated in a study at NYU.

In the replication (Kaufman, Butensky, and Wiliamson, 1989) we found that the amplitude of N100m changes with ISI up to 16 sec in about the same manner as that of N100 at Cz, provided that N100m is recorded over the left hemisphere. However, recording it over the right hemisphere results in saturation of the ISI effect after 4 sec. This was done with 7 subjects. It suggests the the "memory" of the left temporal lobe is longer than that of the right, and this may well have something to do with language function. The paper by Kaufman et al. (1989) was presented at the International Biomagnetism Conference in August 1989. It should be noted that this paper raises some problems for the view that

magnetically silent sources must contribute to the endogenous N100. It may also be related to a recent finding made under the aegis of another AFOSR grant that N100m amplitude detected over the right hemisphere decreases in amplitude with the size of the memory set of tonal stimuli in a Sternberg-like task. However, this same effect is apparently absent over the left hemisphere. Clearly, this is a topic for further investigation.

P300 Studies

In another study early in the project we joined forces with E. Donchin and his colleagues from the University of Illinois in a study to replicate our original observations of the P300 phenomenon (Okada et al., 1982a). The significance of P300 for cognitive processes related to workload is made clear by McCarthy and Donchin (1981) and by Isreal et al. (1980), for example. The main reason for attempting a replication is that controversy surrounds the interpretation we gave to our original data, namely, that the hippocampal formation is the most likely source of P300. We set out to replicate the McCarthy and Donchin study using the PEARL system from the University of Illinois, together with their software, in acquiring and anlyzing the data. Owing to a high level of ambient magnetic noise at low frequencies, a very large number of trials was needed to obtain enough data for detecting P300m. Therefore, we did not completely replicate McCarthy and Donchin, but we did complete a set of visual odd-ball trials and were able to map the extracranial magnetic field associated with P300. This map confirmed our earlier study in that the equivalent current dipole source was located in or near the hippocampal formation. Since the completion of that experiment, a magnetically shielded room and improved instruments (funded by the DOD-University Research Initiative Program at NYU) were installed in the Neuromagnetism Laboratory and we began to acquire P300m data. This work, which was done in collaboration with E. Donchin, did not live up to its early promise, since subjects proved to be unstable over time.

In this experiment we used a standard odd-ball paradigm in which subjects had to keep count of infrequently occurring events presented in via either visually or aurally. In the earlier trials we did see P300m responses of substantial amplitude. However, in order to fully map the field so that we could compute statistically significant dipole fits, the 5-channel neuromagnetometer had to be moved to a very large number of different locations, and many replications were needed at each of these locations. Since we were essentially discarding 80% of the trials (where no odd-ball was presented), this was an extraordinarily inefficient experiment. Furthermore, owing to the long period of exposure to the same conditions, subjects habituated to the paradigm and the P300m became very unstable. In an attempt to rescue the data we made use of several time-consuming procedures. These included rescaling each P300m using each electrical P300, under the assumption that its changes would be correlated with changes in P300m. To make a long and sad story short, none of this satisfied us, and we had to conclude that the experiment was inconclusive.

We were reluctant to abandon this important endeavor, so S. Curtis, E. Donchin and L. Kaufman continued to meet and planned further experiments. We decided to employ a new paradigm that had recently been developed in Dr. Donchin's laboratory, since it allowed us to obtain P300 responses on each trial, permitting the use of all of the data and not merely the odd-ball trials. In their paradigm, Donchin and his colleagues presented letters, i.e., an 'S' or an 'H', with a dot placed either at the top of the letter, in line with the cross-bar, or at the bottom of the letter. With the dot near the top of an H, the next letter to be seen would have an 80% of being an H. The middle dot indicates that there is a 50:50 chance it would be an H or an S. The bottom dot indicates that the next letter would most

likely (80%) be an S. We adopted this procedure, and also added an auditory condition in which a tone is presented along with one of higher pitch, the same pitch or a lower pitch, to indicate that the next tone would have either a high, low, or intermediate probability of being the same as the preceding main tone. Prior to the end of this project we completed behavioral studies to show that RT was the same for both the visual and auditory stimuli. We also demonstrated that it is possible to detect P300m relatively easily by averaging responses to the "target" letter, the one predicted by the subject, over all trials. The field pattern obtained on one subject is consistent with a common source for both the visual and auditory P300s. Furthermore, the locations of the field extrema were similar to those reported earlier by Okada et al. (1983). Unfortunately, this experiment was not quite complete at the end of the project, but it is being continued under another grant. Data collection was initiated during the spring months, and was conducted intermittently since then. It will be resumed in September and completed by November, at which time we plan to submit a paper for publication. A copy of the MS will be transmitted to AFOSR. It should be noted that a preliminary report on these more recent developments was given by E. Donchin at the Carmel meeting in January, 1989.

Chrominance Channels

Krauskopf, Klemic, Lounassmaa, Travis, Kaufman, and Williamson (1989) reported on the results of a study to determine whether pure chrominance changes affect cortical areas that are not affected by luminance changes. (Travis was a post-doctoral student supported by the URI, and Klemic a graduate student.)

In color vision the first stages, at the level of the receptor mechanisms, are now fairly well understood, and research by Krauskopf and his colleagues in the psychophysical domain (Krauskopf, Williams and Heeley, 1982) and the physiological domain (Derrington, Krauskopf and Lennie, 1984) has helped to clarify the nature of the second stage opponent mechanisms. It is clear that the parvocellular lateral geniculate layers consists of two major types of center-surround chromatically opponent units. Lennie, Sclar, and Krauskopf (1985) applied the same electrophysiological methods to cortical units as were used to study lateral geniculate units, and found cells tuned to respond best to isoluminant stimuli in many different directions around the color circle. Detailed analysis of psychophysical habituation experiments and results of experiments on the discrimination of threshold changes in color also point to the existence of higher order mechanisms tuned to many different directions in color space (Krauskopf, Williams, Mandler, and Brown, 1986).

Dr. Krauskopf continued to study these higher order mechanisms using psychophysical and physiological procedures. In the last year of the URI he has made use of the 5-channel system at the Neuromagnetism Laboratory at NYU and introduced the use of isoluminant chromatic stimuli to determine if it is possible to detect spatially separated regions in visual cortex that are tuned to respond to the different directions in color space. Thus far, microelectrode studies have not clarified this issue. In this work isoluminant red and green stimuli were presented alternately. Also, increments and decrements in luminance of white patches on a neutral background are similarly alternated. The chromatic stimuli, which are matched by means of heterochromatic photometry to their neutral backgrounds, evoked rather robust neuromagnetic fields. Mapping these fields in the occipital region showed activity of apparently common sources for both the chromatic stimuli and for the luminosity stimuli. However, with more extensive mapping it appears that spatially distinct sources may be activated by changes in luminosity as compared to changes in chromaticity. This separation of function is not apparent in early components of the evoked

response, but is apparent in later components with sources outside the primary visual areas - especially for sources of responses to changes along the red-green axis. While blue-yellow pairs of stimuli have also been used, insufficient data were collected to allow statements about their sources.

The foregoing work required the generation of isoluminant stimuli using a video projector to form the images of the stimuli on a screen inside a shielded room. This was not a trivial exercise. The general approach was to use time varying stimuli in which the chromatic content was varied so that they exhibit either a purely luminance variation or purely chromatic variations in different directions within an isoluminant plane. The goal was to find regions of the cortex that respond strongly to stimuli varying in different directions in color space. Although the data are fairly meager, it is clear that stimulus production was successful, and that it is indeed possible to obtain responses and locate the sources of these responses.

While this work was promising, it was not conclusive, as one subject showed separately activated channels, but data of a second subject did not. One explanation for this is the possibility that the difference in field patterns for one subject comes from activity shifting across cortex where it forms a gyrus, while for the other the cortex is essentially flat. Magnetic studies are exquisitely sensitive to rotations of the current dipole representing the aggregate direction of activity, and this may have been detected in the former subject. Because of the attractive features of this study, Gladys Klemic was invited by Dr. Lounasmaa to work at his Low Temperature Physics Laboratory at the Helsinki Technological University, with his Laboratory's financial support. After a three month stay in Helsinki, Klemic returned with some new data obtained with a 24-sensor system, but these as well were inconclusive. While this was the stage of the work at the end of our project, we are still giving some thought to this problem.

One possible difficulty is that the separate use of chrominance and luminance stimuli allows too much time to go by. Owing to subject adaptation, the subject's state changes from one block of trials to another, thus masking subtle differences in field distributions. To overcome this potential difficulty, it is possible to present alternating colors at a steady-state frequency of, say, 4 Hz. At the same time, the luminance of the target stimulus is made to change at a frequency of 7 Hz. While the particular temporal frequencies are to be determined empirically to insure the strongest possible response at the highest possible fundamental frequencies, it is important that they not be related harmomnically, i.e., one must not be an integer multiple of the other. In that case, the responses to luminance change can be computed independently of those to chrominance change, especially since any shared higher harmonics of the two fundamental stimulus frequencies would be outside the range of appreciable brain responses. Thus, in the case of 4 and 7 Hz as stimuli, the first common harmonic is at 28 Hz, and a response to a stimlus presented at 28 Hz is generally quite weak. In any event, this procedure would allow for measuring responses to concurrent chrominance and luminance stimuli, thus obviating masking effects of differential adaptation.

The foregoing idea, and other suggestions as well, was forwarded to Dr. Lounasmaa and it is possible that the Helsinki group will follow through with another experiment. One of his postdoctoral students will visit our laboratory in August, 1990, to discuss various prospects.

Localization of Sources of Long-Latency Auditory Evoked Magnetic Fields

Neuromagnetic studies of Pelizzone et al. (1984, 1985) demonstrated that the neural source of the N100m transient component to a 1-kHz tone burst was laterally displaced in the subject's head by about 1 cm posterior to the region that responds to steady-state stimulation at the same frequency. This showed that individual active regions of auditory cortex may be resolved, suggesting the possibility that spatial separation of the sources of other transient components may also be established. To determine to what degree this may be attained, one of us (S.J. Williamson) collaborated with the neuromagnetic group at Los Alamos National Laboratory to carry out systematic measurements with a single-sensor SQUID system of the responses to long tone bursts. This was the first quantitative analysis to determine the positions for the equivalent current dipole sources for all four long-latency components (P50m, N100m, P200m, and the steady field). All sources were found at positions indicating they lie near or in auditory cortex, consistent with published results for N100m and P200m. This has now been confirmed in an independent study by Papanicolaou et al. (1989).

A strong effect of stimulus frequency was found for the position of the source of P50m, but remarkably there were no consistent trends to the direction of the source's shift with stimulus frequency. This finding would appear to demonstrate important individual differences for the functional map of human auditory cortex. The P200m source is generally weaker than that of N100m and in some subjects may overlap the early portion of the steady field. The position of the source of the steady field could not be distinguished from that of N100m. There was, however, a clear separation of the sources of P50m and P200m from N100m. These results have been reported by Arthur et al. (1987).

Visual Spatial Attention

In view of the fact that this particular research was not completed until the very end of the URI program, and that little prior atention was given it in previous reports, we treat it here in somewhat greater detail than we did the research summarized above. What follows is a preliminary asessment of teh results. The final version will be submitted as an addendum to this Report in the form of a manuscript for publication.

Introduction

It has been known for some time that the attention a subject pays to various visual, auditory, or tactile stimuli modulates the electrical responses to those stimuli recorded from scalp elecrodes. Effects of directing visual attention to specific directions in space on event-related potentials (ERPs) were first reported by Eason et al. (1969). In that study, subjects were presented with small flashes of light which could occur 20 degrees of visual angle to the left or to the right of a fixation point. They were instructed to pay attention, without moving their eyes, to flashes occurring at only one of the two locations, and to press a button as soon as they detected a flash occurring there. In occipital ERPs, two positive peaks with latencies of 120 and 220 ms In occipital ERPs, two positive peaks with latencies of 120 and 220 msec and two negative peaks of 170 and 270 msec latencies were evident, and their amplitudes were greatly enhanced in the attended condition relative to the unattended. Van Voorhis and Hillyard (1977) repeated this experiment with a slightly different task. Rather than simply detecting flashes at the instructed location, subjects had to discriminate single (non-target) from double (target) flashes. In response to non-target stimuli occurring at attended locations, ERPs at occipital electrode sites included positive peaks with latencies of 100 and 220 msec which were significantly larger in amplitude than

responses occurring when the same locations were ignored. In this study, the negative occipital peaks showed no amplitude differences across attention conditions. However, in other studies where spatial attention was manipulated (e.g., Eason, 1981; Hillyard and Munte, 1984), both negative peaks exhibited significant effects of the attention condition on their amplitudes.

Hillyard and Mangun (1988) described the typical effect of directing spatial attention on the ERP responses to stimuli at a particular location as the relative enhancement of the amplitudes of some or all of four occipital components, P1-N1-P2-N2, occurring between 100-300 msec after stimulus onset, with no effect on their latencies. As these components occur whether the stimuli that evoke them are attended to or not, it was suggested that they reflect the obligatory initial sensory processing that occurs with the presentation of any stimulus in the visual field. The relative enhancement of amplitude of the responses to attended stimuli is presumed to be indicative of increased neural activity, and could reflect a gating or selection process in which the attended stimuli undergo a greater amount of early sensory processing.

Such an interpretation is of considerable interest in the study of human information processing. That some stimuli can be attended and other simultaneously occurring stimuli can be effectively ignored has been studied in modern psychology beginning with Cherry (1953). The level of processing at which attentional selection can occur has always been a central issue to structural theories of attention (see Broadbent, 1982; Johnston and Dark, 1982). Some theorists (Broadbent, 1958,1971; Triesman, 1960) proposed that attentional selection can occur in early sensory processing by filtering out or attenuating unimportant stimuli. Others (Deutsch and Deutsch, 1963, Norman, 1968) countered that selection does not act on perceptual processing. Instead, all stimuli are completely analyzed and "selection" is the reflection of the relative weighting of these analyzed stimuli in response decisions. Research using behavioral indices has not been successful in conclusively differentiating between these rival theories of selection. Thus, the suggestion from ERP data that some of the earliest cortical perceptual processing is affected by attention is quite interesting. However, this remains only a suggestion until several issues are resolved. One is whether early-occurring components of the *average* ERPs show the effect of attention without being influenced by later stages of neural processing. Feedback associated with these later stages could influence the effective "gain" of activity in more peripheral stages *after* perceptual analysis had occurred. This would be totally consistent with theories such as those proposed by Deutsch and Deutsch, for example. Also, the cortical locations of the sources of the affected ERP components are not yet known. To establish a claim of early selection based on visual ERP results, changes due to selection must be found in the more initial stages of the visual processing pathways, for example the striate cortex, the first cortical area devoted to visual processing. This region was suggested by Hillyard et al. as the neural source of early ERP components affected by attention. On the other hand, Harter and Aine (1984, 1986) proposed that the ERP data indicated a source in the parietal areas for visual spatial selection. Unfortunately, interpretations of source locations of electrical activity based on a small number of electrodes are not reliable (Nunez, 1981a,b).

Using 16 electrode sites covering the back of each subject's head, Hillyard and Mangun generated plots of isopotential contours by averaging data over a number of human subjects. These plots suggest the source of the P1 component is in primary visual cortex, which supports their conclusion that sensory gating must occur at or below this level. Mangun and Hillyard (1990) also produced contour plots for P115 which indicated a source in lateral extrastriate cortex, and suggested that this implied that selection processes

occurred prior to this site, in primary visual cortex or in subcortical structures. Unfortunately, if the contour plots are based on "grand means", then it is impossible to take into account the radical differences among subjects in head shapes and sizes, as well as the large anatomical differences in size and location of visual cortex between subjects (Stensaas et al., 1974). Hence, it is impossible from these plots to be certain of the distributions of potentials about the scalp or to infer their source locations. However, the data do suggest that the generators of early components are located in the occipital or parietal portions of the brain. By extension from the fact that the source of the magnetic N100 component is clearly located in auditory cortex (Hari et al., 1980; Curtis, et al., 1988), the analogous response components also arise in visual cortex. However, this remains to be verified for the visual system. Such a result would be significant also because while electrophysiological recordings of single cell activity in other primates have established that attentional processes function in extrastriate visual areas, notably V4 (Desimone et al., 1988) and parietal areas (Mountcastle, 1980), such studies of primary visual cortex have produced mixed results (Moran et al., 1984, Haenny et al., 1988). Also, the later components affected by attentional states probably do not arise from visual cortex, but the locations of their sources are even more unclear, and need to be elucidated.

Of course, attention is not a simple process, and knowledge of the information processing level at which selection occurs is only part of the story. Attention has often been viewed as a limited resource which may be allocated differently, depending on the strategy employed by the subject, as well as the demands inherent in the task. In many situations attention can be viewed as the outcome of the application of several different resources that can be applied more or less independently to several concurrent tasks. Here too the strategies adopted by subjects are of considerable importance.

One approach to understanding this complexity is the application of a methodology having its origins in the theory of signal detection (Green and Swets, 1966). In particular, the Receiver Operating Characteristic (ROC) has been adapted to the study of resource allocation in situations in which attention must be applied differentially to two concurrent tasks (Norman and Bobrow, 1975; Kinchla, 1980; Sperling and Dosher, 1986). When applied to such situations the ROC curve becomes the so-called *Attention Operating Characteristic* (AOC). Most commonly, the data used to generate AOC curves are behavioral, e.g., reaction time (RT), accuracy, etc. Mangun and Hillyard (1987) extended this approach to include ERP data rather than explicit behavioral data in the study of attention. Considering the ERP and the overt responses associated with different locations to be different tasks, they plotted amplitude data related to early components (earlier than 180 msec) from both spatial locations in the form of AOC curves. These curves did not correlate with the behaviorally-based AOC curves, although late ERP components recorded over parietal and occipital areas did so correspond. It should be noted that evidence exists that deep structures in or near medial temporal cortex may contribute strongly to late ERP components (Okada, Kaufman and Williamson, 1983), so it is impossible to conclude from the data of Mangun and Hillyard that the sources of these components in their experiment are indeed located in either parietal or occipital cortex. Moreover, when subjects in the Mangun and Hillyard experiment divided their attention between two spatial locations, the AOC curves generated by plotting their behavioral indices indicate that attending to one location does not interfere with attending to a second position. It should be noted that task difficulty was not manipulated, and the tasks used by Mangun and Hillyard were relatively easy for subjects to perform. Thus, even though there were no decrements in performance indicative of a limited resource required by both tasks, it is premature to conclude from

their data that independent attentional resources were applied to different spatial locations.

In view of these questions, it would be of considerable interest to devise similar tasks that interfere with each other in varying degrees, as indicated by behavioral data, and determine how this is reflected in the activity of the brain. In addition, it is equally interesting to identify at least some of the loci within the brain whose activity is differentially modulated by allocation of attention.

The neuromagnetic method has been successful at locating neural sources with a high degree of spatial resolution (Yamamoto et al., 1988). The same methods have been used to locate cortical neural sources of activity in response to auditory, somatosensory, and visual stimuli. Given this spatial resolution achieved by Yamamoto et al. in locating the source of N100, which is affected by attention, this technique appeared ideal to study physiological responses to visual stimuli during modulation of spatial attention.

In our first experiment, the paradigm used with success in ERP studies of visual spatial attention was implemented, and magnetic field measurements were made in order to find a neuromagnetic effect of spatial attention and to map the field patterns and use them to locate sources of components affected by attention. Field patterns were compared with theoretical patterns associated with equivalent current dipoles located in different parts of the brain in order to find the cortical regions that contributed to attention effects. In the second experiment, subjects performed a discrimination task that was made more difficult, in order to observe how this might change the resulting attention effects from those found using a simpler task.

Experiment 1

Method

Three paid graduate students participated in this study. All had normal uncorrected vision and all were right-handed. Two were female, and one was male. All were in their early twenties. The visual stimulus was a square field one degree of visual angle on a side containing either 2 or 4 parallel vertical bars. This square field was presented just above the horizontal meridian, and centered either 5 degrees to the left or to the right of a central fixation point, which was a white cross 0.5 degrees wide. The bars were alternating black and white, each slightly less than one log unit below and above a background gray luminance of 0.68 cd/m^2). All bar patterns were presented for 34 msec with an average ISI of 1100 msec with a random variation of as much as 250 msec. In all experiments a 4-bar display or a 2-bar display was presented either to the left or to the right of fixation with a 50% probability. The 4-bar pattern had either a 20% or 50% probability of appearance on a given side. Stimuli were generated using a Commodore Amiga computer and projected into a magnetically-shielded room with an Elektrohome video projection system.

Procedure

Subjects were seated on a comfortable kneeling chair facing the projection screen, leaning forward onto head, chest, and forehead supports to achieve a stable position. The importance of maintaining eye fixation on the central white cross throughout the run was stressed. Before each block of trials, subjects were instructed to focus attention exclusively on either the left or right stimulus location. The subject's task was to press a button with their right hand whenever the 4-bar stimulus was detected at the designated location. This stimulus had a 20% chance of appearing on either side. In each block, trials continued until at least 100 had occurred at each location. At each probe location from which

magnetic measurements were taken, at least two blocks of trials were run - one preceded by an instruction to focus attention on the left location and respond only to target stimuli there, and another preceded by an instruction to attend to and respond to targets only at the right location.

Recordings

Magnetic field measurements were made using a multisensor probe incorporating 5 SQUID-based second-order gradiometers, each having a 1.5 cm coil diameter and a 4 cm baseline between adjacent coils (for more details, see Williamson et al., 1984). Measurements were made over the entire posterior portion of each subject's head. In the case of subject SS, recordings were made from 34 probe positions, resulting in 170 spatially separate measurements. For subjects BR and JV, 48 and 19 probe positions were used, providing measurements from 240 and 95 locations, respectively. Sensor positions and orientations relative to a head-based coordinate system were determined electronically using the Probe Position Indicator (PPI) system (Biomagnetic Technologies, Inc.). PPI was also used before and after each trial to verify that the subject had not moved more than 2 mm. If he had, the run was repeated.

Source Localization

The outputs of the SQUID electronics were bandpassed between 0.1-50 Hz and then sampled by an HP9000 Model 350 computer at a rate of 128 Hz. Sampling began 100 msec before stimulus onset and continued over a 700 msec recording epoch. Recorded data were digitally filtered from 2-30 Hz, and recorded epochs were averaged selectively by stimulus type and location. Isofield contour plots were then constructed in the following way. Magnetic field amplitudes at a selected instant in time were retrieved from the averaged data along with their associated sensor positions. Data from across the occipital and parietal regions of the scalp were transferred onto a two-dimensional surface using an azimuthal equal-distance projection. According to this scheme, the midpoint between periauricular positions of the head is taken as the center of a sphere; and distances from this origin along any great circle are indicated by the same distances from the origin across the flat graph. These data are used by a program that performs Laplacian and spline interpolations and generates isofield contour maps. The angular separation between the field extrema on the surface of a sphere that best fits the subject's scalp gives the position and depth of the current dipole that accounts for the observed field pattern (Williamson and Kaufman, 1981). For greater accuracy, a computer program is also used to obtain the parameters for the current dipole whose field pattern best fits the observed pattern. This also provides a best-estimate for the uncertainty in the parameters from an analysis based on the chi-square distribution.

Behavioral Measures

In order to have an objective indication that variations in amplitudes of components of the field were indeed due to the fact that subjects directed attention to one position and ignored the other, the reaction time (RT) and accuracy of judgment were recorded.

Results

Behavioral Results

None of the subjects found the task particularly difficult to perform. Both subjects SS and BR performed at 97% or better accuracy levels whether attention was focused on left or right locations. Subject JV fared a little worse, obtaining an 83% accuracy level. There was no suggestion in the RT data of premature reactions nor of RTs that were obviously too long.

Neuromagnetic Data

All three subjects responded similarly to the visual stimuli in that their event-related fields (VERFs) contained as many as six components, as illustrated in Fig. 1a, depending upon the positions of the sensors. These data verify the occurrence of an attentional effect in the VERF. When attention is allocated to one position, left or right, some of the responses to the nontarget stimuli at that position are enhanced relative to the responses to the nontarget stimuli when that same location is ignored. This effect is most robust for components having latencies longer than about 200 msec. The earliest (110 msec latency) component never shows a significant attentional effect, but the components between 110 and 200 msec show an effect, but only at some positions.

Contour maps showing the field patterns associated with a component occurring 120 msec after stimulation are shown in Figs. 2 and 3. Both maps contain two field extrema, which have virtually identical locations for both the attention and ignore conditions. From this we may infer that there were no eye fixation displacements large enough to significantly change the location of the activity associated with the stimulus. For this subject (SS), the two field patterns remain in good registration, which proves that the cortical source of the field did not shift between conditions. It should be noted, however, that in this case there is no atentional effect on the strength (current dipole moment) of the underlying source. These plots indicate that the particular source that best accounts for them is located approximately 3 cm above the inion and 3 cm to its right. Since the stimulus was located in the left visual field, it would appear that the source is located in or near striate cortex. This is consistent with the results for the other two subjects.

Generally, the later components show an appreciable effect of attending. This is most pronounced for a component occurring about 240 msec after stimulation. This is apparent in Figs. 1a and 1b in which the component peaking at 240 msec is stronger under the attend condition (solid line) than under the ignore condition (dotted line). Fig. 4 is a contour plot based upon measurements of the field made 260 msec after stimulation. It resembles those plotted at several other nearby latencies before and after, and it clearly illustrates the complexity of the problem of identifying neuronal sources for these later components. The field pattern was based on measurements made while the subject was attending to the right-hand location. If the source had been located in primary visual cortex, it would have to be in the left hemisphere. However, this complicated field pattern contains evidence for more than one source because there are three clear field extrema: a positive extremum at position (-3,0) and negative extrema at (8,0) and (-4,9). These could be interpreted as representing two dipole sources. One is indeed in the left hemisphere, horizontally oriented and located about 3 cm to left of midline and 5 cm above the origin (i.e., 10 cm above the inion). The other is in the right (ipsilateral) hemisphere, oriented almost vertical and positioned about 6 cm to the right of the midline and at the origin (about 3 cm above the inion. When the subject ignores the same right-hand position in visual space, the resulting field pattern is reduced by 30-40% in amplitude, with no obvious changes in the source positions.
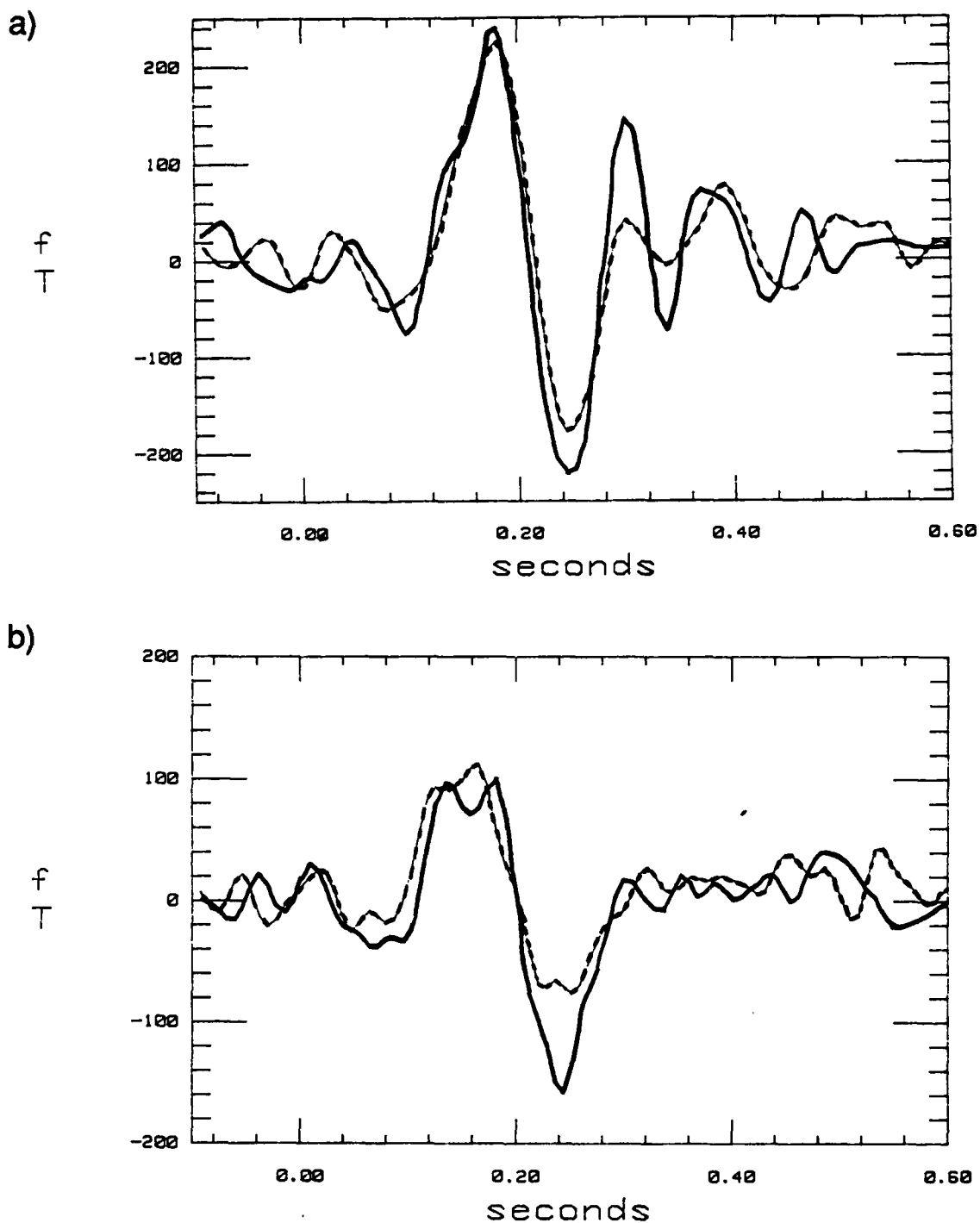
Figure 1. (a) Averaged visually evoked field from a sensor positioned over the occipital area of subject BR. The solid line shows the response to nontargets in the left location when they were attended, and the broken line shows the response when they were unattended. (b) Averaged visually evoked field at the same location with non-targets in the right location.
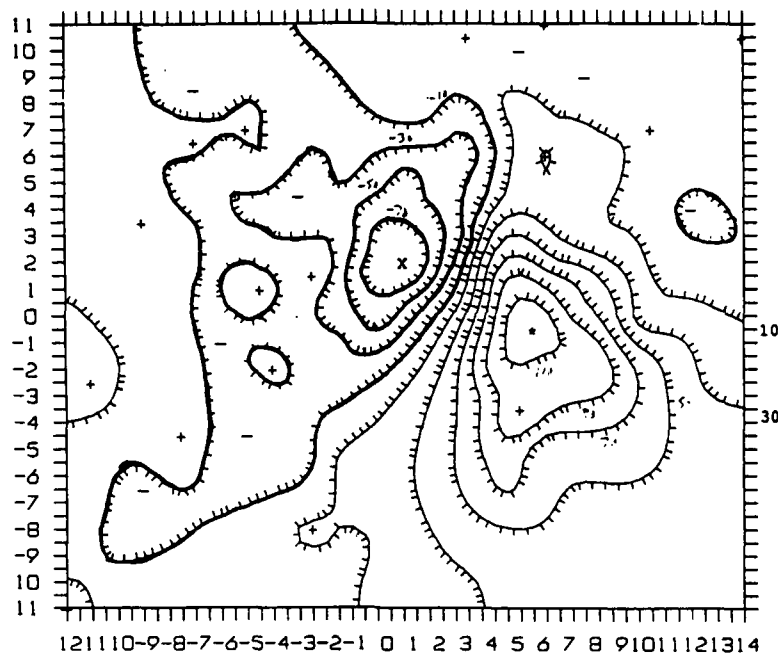
Figure 2. Isofield contour plot of responses from Subject SS at a latency of 119 msec after stimulus onset at the left location in the case when the left location was attended. Each contour represents an increment of 20 fT, and the thick lines represent positive field polarity, where the field emerges from the head. The midline of the scalp is perpendicular to the horizontal axis and intersects it at 0; the inion is about 2-3 cm below this origin. Increments in distance along each axis are 0.5 cm.

Figure 3. Isofield contour plot for the same subject and latency as in Figure 2, but for stimuli at the left location that were ignored.
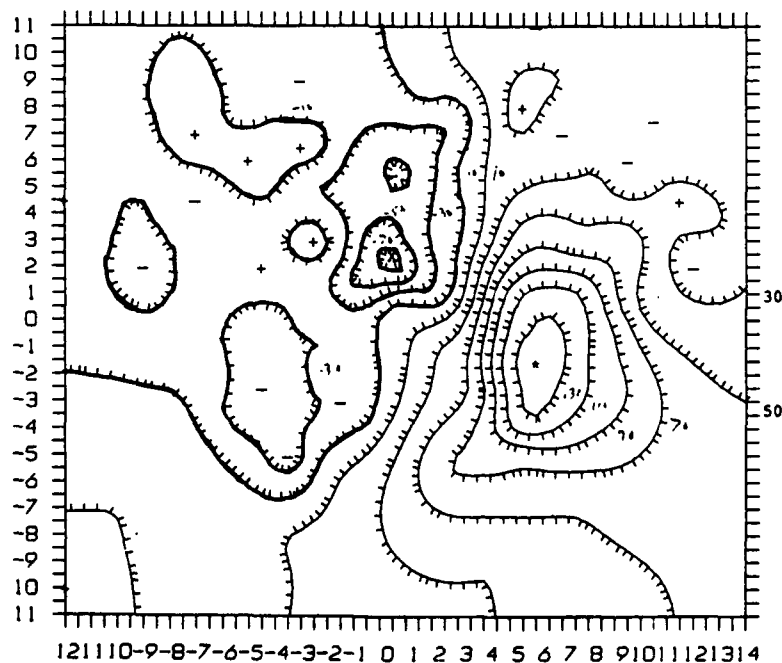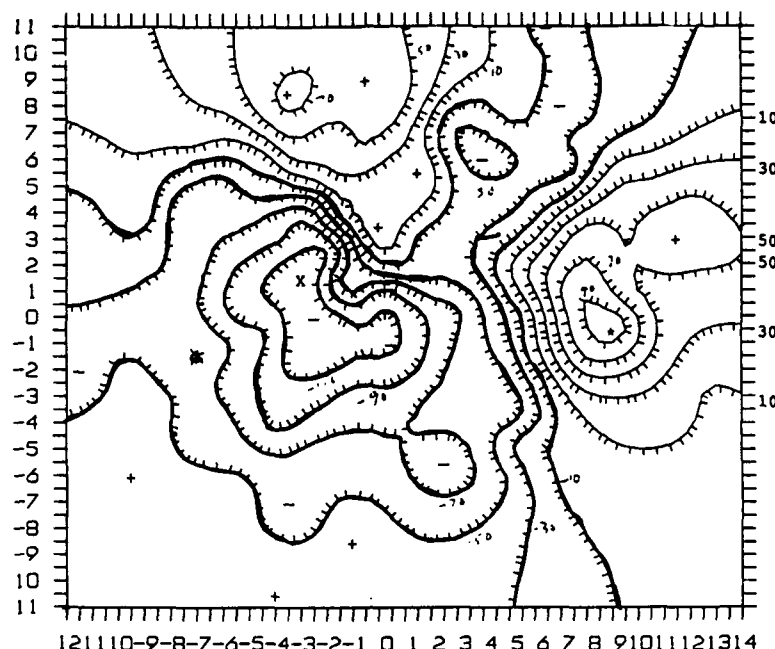
Figure 4. Isofield contour plot for Subject SS at a latency of 259 msec after stimulus onset to nontarget stimuli in the right location when that location was attended.

While caution must be exercised in evaluating such complicated multipolar source configurations, it is possible to make some tentative inferences about which regions of the brain are active at the same time. Thus, in the case of this component, it seems clear that the ipsilateral cortical area 18 or 19 may be active while the contralateral parietal region is also active. It is to be noted that multipolar distributions were encountered for all of the later components of the VEF. Therefore, simple single source solutions to the inverse problem, such as those suggested by Mangun and Hillyard (1990), are not appropriate for dealing with this problem. Isofield or isopotential contours reflecting the presence of a simple dipolar source (which is what Mangun and Hillyard reported) are incomplete. A principal components type of analysis would be a reasonable approach to further evaluation of these data.

The salient components peaking about 140 and 180 msec after stimulation show weak and inconsistent attentional effects. These effects are undoubtedly of great importance, since they indicate the presence of modulation of activity of earlier stages by attention. However, they clearly do not vary sufficiently in amplitude with attention to "explain" the stronger effects on later-occurring components. That is to say, if the various components reflect a sequential (serial) set of processes, the effect of attention on the earlier ones does not account for the effect of attention on the later ones. This implies concurrent processes that are not reflected in the event related fields.

EXPERIMENT 2 (Division of Attention)

Method

The same three subjects used in experiment one were used in this experiment. Two tasks were used to reflect two different levels of complexity. The first was the same task as in Experiment 1: press the right hand button whenever the 4-bar stimulus is detected at the designated location or locations. In the simpler version of the task the subject responded to the target whenever it occurred at the designated location. In the more complicated version of the task the subject was to press the button only after a second 4-bar pattern on the appropriate side had occurred.. This required remembering what was done the last time a 4-bar pattern occurred at that location. This had the effect of making the task pair truly concurrent (see Sperling and Dosher, 1986). In this task pair, both 4-bar and 2-bar patterns occurred with equal frequency. This change in probability was made in order to keep the number of responses in the second task pair approximately equivalent to the number of responses made in the first task pair in each block. Other than this change, the stimuli and their method of presentation are exactly the same in both task pairs. This implies that any changes in physiological response between the tasks is due only to the cognitive demands of the task.

Again, subjects were seated facing the projection screen, leaning forward to rest on chest and forehead supports to achieve a stable position. The importance of maintaining eye fixation on the central white cross throughout the run was stressed. Before each block of trials for either task pair, subjects were instructed to focus attention exclusively on either the left or right stimulus location, or to divide attention between the two locations. In the second case, the subject was to divide his attention equally or to emphasize one side more than the other. Thus five attention allocation conditions were used: focused left, emphasize left, equal division, emphasize right, and focused right. These conditions resulted in responses to stimuli on each side in which the allocation of spatial attention was split approximately as follows for left and right respectively: 100%/0%, 75%/25%, 50%/50%, 25%/75%, and 0%/100%. Payoff schedules were used in order to clarify these allocations. In the 100% allocation condition, subjects gained 12 cents when a target was correctly responded to, and lost 12 cents if a target was missed or a false alarm was made. In the 75% condition, a 9-cent figure was used in the same way; and in the 50%, 25%, and 0% conditions, the pay-off rates were 6, 3 and 0 cents.

Recordings

The probe was centered on locations near the midline on the back of the subject's head where strong responses were produced in previous recording sessions. Sensor positions and orientations relative to a head-based coordinate system were determined electronically using the PPI system. Through the use of this system, the probe could be replaced to the same location on the head within a few millimeters. PPI was also used before and after each run to verify that the subject had not moved more than 2 mm. If he had, the run was repeated.

After each probe positioning over the scalp, four to six blocks were run for each allocation condition. Recordings were made over 2-3 days for each task pair, with the first task pair completed before the second was taught and run. It should be noted that the 75%/25% allocation conditions were not run for the first task pair for subject SS, and that subject JV did not perform the second task pair.

Analysis

Re-positioning of the probe was done imperfectly despite the best efforts of the experimenter. As a result, not all sensor locations from which data were taken coincided over all

allocation conditions. Nevertheless, if a criterion distance of less than 0.7 cm was used, each subject had 4 to 5 sensor locations containing from 2 to 6 blocks of averaged neuromagnetic responses for each allocation condition. All subjects were analyzed separately. For each waveform, peak amplitudes at a number of latencies (corresponding to obvious components) were chosen. For each attention allocation condition for each location, the chosen amplitudes were weighted by their signal-to- noise ratio (mean amplitude/standard error of the mean) and were combined in a weighted average. These weighted mean amplitudes were then combined across the 4 or 5 sensor locations. This combination was also a weighted average (with the coefficient for each number being itself divided by the straight mean of all the locations). The resulting weighted amplitudes for each component (over right and left stimulus locations and for each subject) were entered on a table and also plotted (allocation condition vs. amplitude).

Results

Behavioral Performance

Table 1 summarizes the accuracy and reaction time data for each of the three subjects for each attention allocation condition in both tasks. All subjects found the first task quite easy in the focused conditions, and suffered only marginal decrements in accuracy and RT when asked to divide their attention over both locations. In the second complex task (Table 2), however, two subjects had very large decrements in accuracy when asked to divide their attention equally between the two locations. Subject SS showed increasing RT and decreasing accuracy as less and less attention was allocated to both left and right positions. Subject BR showed a similar trend with one exception. In the case of an approximately 75-25% split in allocation, accuracy for the de-emphasized location is as high as accuracy when attention is divided evenly. In this case however, this subject's number of false alarms in response to stimuli on the 75% side rose dramatically, and RT fell below that of the focused condition. This suggests that the subject responded to instructions to emphasize one side at the expense of the other in an unexpected way, lowering his criteria for deciding on targets on the emphasized side in an attempt to maintain performance at the de-emphasized location.

The accuracy data obtain in the simple task are presented as AOC curves for the three subjects in Fig. 5a-c. It is obvious from these curves that subjects perform nearly equally well regardless of how they allocate attention. For example, when a subject attends exclusively to one position and ignores the other, he does no better in detecting targets at that position then he does when he also allocates a portion of his attention to the opposite position. This may be taken to be an instance of tapping independent resources when monitoring different locations in visual space, and it is similar to results described by Hillyard and his colleagues. It is to be noted that the AOC curves based on RT data are quite similar except for one anomalous point that will be dealt with in our forthcoming publication.

Now let us consider what happens to these data when subjects perform the more complicated task. In the case of subject SS, the AOC curve (Fig. 6a) approximates a straight lines. This is also true of the AOC curves based on RT data. These results imply a strategy of switching attention from one side to the other rather than a strategy of sharing resources over all trials (Kinchla, 1979). The curves for subject BR (Fig. 6b) also suggest switching of attention, but the abrupt change in the curve also imply a change in strategy employed by the subject when attentional allocation is at intermediate levels. These results

Table 1

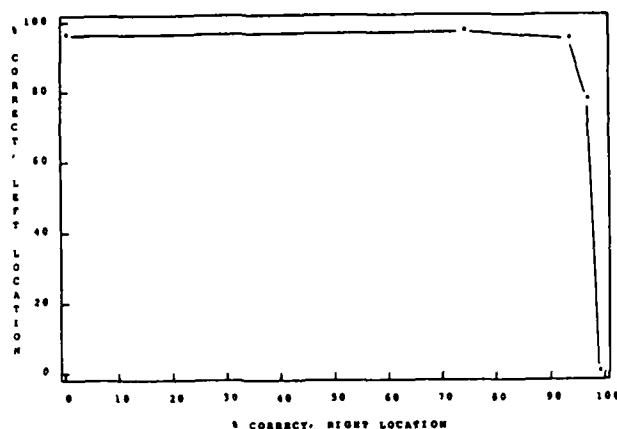### Performance in the First Task Set (Simple Discrimination)

	Left Location % Attention Allocation				Right Location % Attention Allocation			
	100	75	50	25	100	75	50	25
Subject BR								
% Correct	96	97	95	77	99	97	93	74
False Alarm Rate (%)	2	3	0	1	1	1	2	0
Mean RT (msecs)	402	396	410	443	404	389	407	449
SD (msecs)	3	4	3	4	3	3	4	4
Subject SS								
% Correct	99		94		97		95	
False Alarm Rate (%)	1		0		0		1	
Mean RT (msecs)	408		396		392		392	
SD (msecs)	3		4		4		4	
Subject JV								
% correct	82	79	74	55	84	67	71	61
False Alarm Rate (%)	2	1	0	3	1	3	2	1
Mean RT (msecs)	470	456	440	484	477	462	424	478
SD (msecs)	6	5	5	6	6	6	7	5

Table 2

Performance in the Second Task Set (Complex Discrimination)

	Left Location % Attention Allocation				Right Location % Attention Allocation			
	100	75	50	25	100	75	50	25
Subject BR								
% Correct	93	79	69	70	95	85	63	62
False Alarm Rate (%)	3	24	7	4	4	24	15	6
Mean RT (msecs)	436	409	441	440	407	396	455	463
SD (msecs)	5	7	8	8	5	6	9	11
Subject SS								
% Correct	95	74	42	27	88	77	51	25
False Alarm Rate (%)	3	3	5	7	0	2	5	4
Mean RT (msecs)	413	458	482	511	428	450	472	487
SD (msecs)	7	7	9	11	8	7	8	16

a) Subject: BR

b) Subject: SS
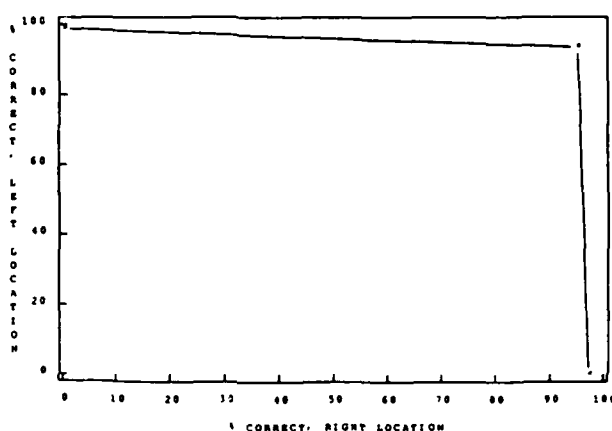
c) Subject: JV
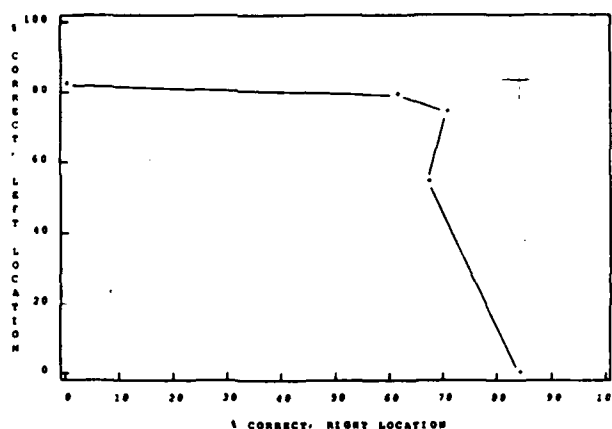
Figure 5. Attention Operating Characteristics (AOCs) using performance accuracy (% correct) for the first task set (simple discrimination). The horizontal axis represents accuracy for one component task, response to targets in the right location, and the vertical axis represents accuracy in the other component task, response to targets in the left location. data for three subjects for the easy task. The points are accuracy data taken from Table 1 in the following pairs for attention allocation to left and right location, respectively: Data for 75%/25% and 25%/75% were not obtained for subject SS.

a) Subject: SS
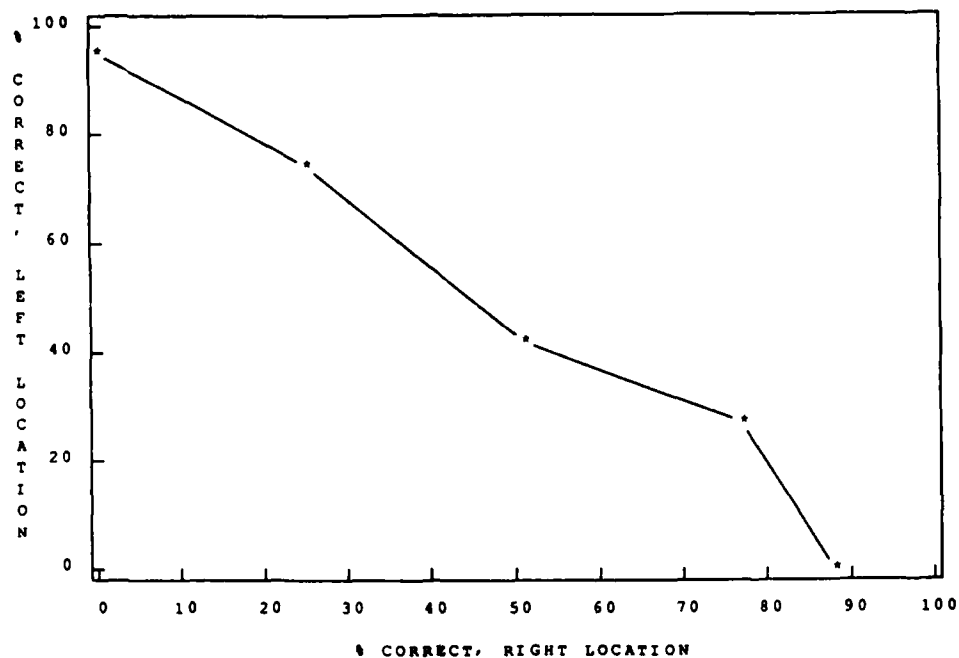
b) Subject: BR
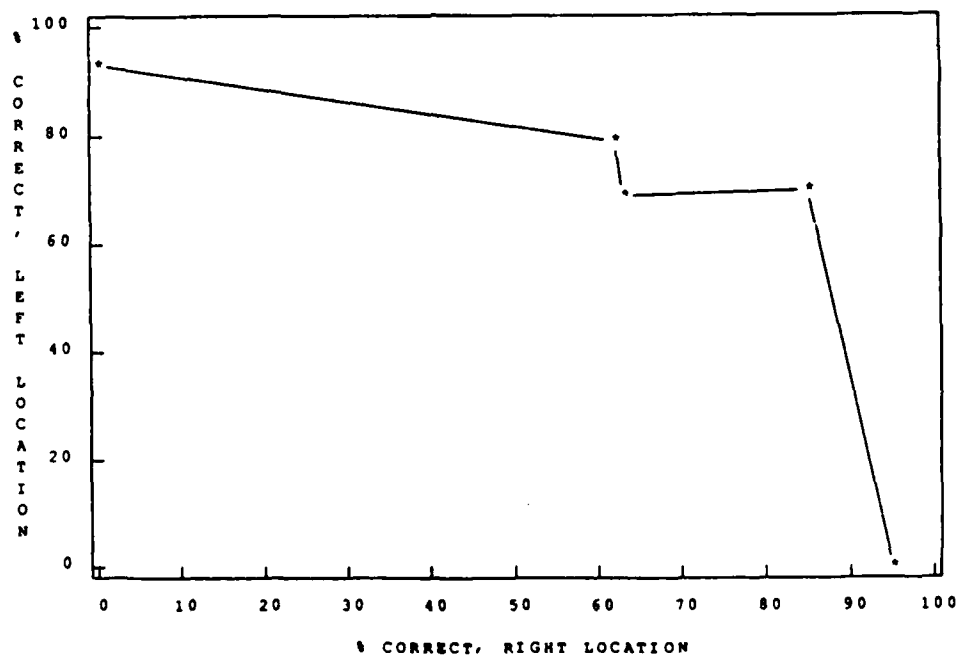

Figure 6. Attention Operating Characteristics (AOC) for subjects SS and BR in the second task set (complex discrimination), with data taken from Table 2. Figure explanation is the same as in Figure 5.

demonstrate that task difficulty must be manipulated to avoid making unwarranted inferences about multiple or single resources being available for a particular attentional task.

The MEG data are particularly interesting. For the first time we report a change in latency of event related field components with task complexity. As illustrated in Fig. 7, the predominant components of the response to stimuli encountered while performing the more complicated task occur about 28 msec prior to the correponding components of the response to the same stimuli encountered in the simple task. We have no explanation for this finding at present, but simply point out that to our knowledge it is the first observation of a latency difference in long-latency cognitive components related to mental workload. This is to be explored in future work.

Mangun and Hillyard (1990) were unable to directly relate ERP amplitudes to their behavioral AOC curves. We faced the same problem. However, by applying the weighting procedures described under the method section, we did find that in the simple task that components occurring between about 200-250 msec after stimulation tended to decrease in
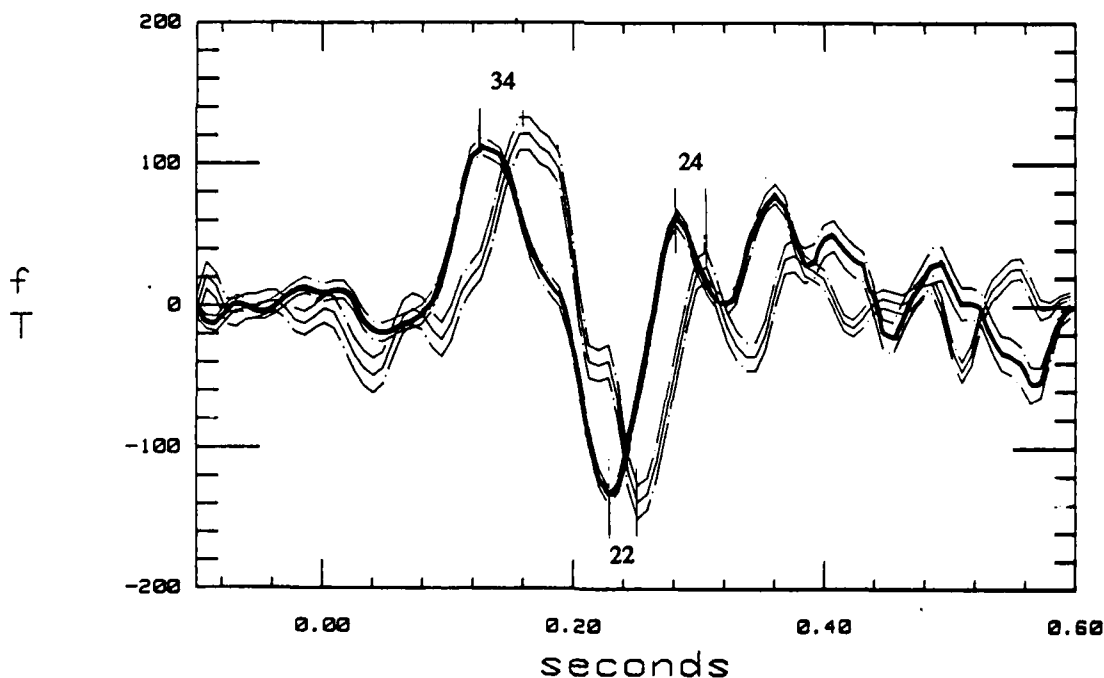
Figure 7. Comparison of averaged event-related fields for subject SS for simple discrimination (light line) and complex discrimination (heavy line). Differences in latencies (msec) for three components are indicated by the numbers within the figure.

weighted average values with the degree of allocated attention. This is shown in Table 3 for the simple task, and in Table 4 for the complex task. However, none of these data, when plotted in the form of AOC curves, mirror the correponding behavioral data. This leads to the general conclusion that the measures of brain activity employed here and in ERP experiments are not complete indicators of the processing involved in selective attention. However, other dimensions of that activity remain to be explored.

Table 3

Weighted amplitudes (fT) of neuromagnetic responses across attention allocation conditions

First Task Set (Simple Discrimination)

Response Latency for Left Location	Attention Allocation Condition				
Subject BR	100	75	50	25	0
135	113	135	121	124	101
185	135	146	96	123	130
244	135	162	94	109	92
300	128	159	102	111	77
350	98	95	60	85	74
Subject SS					
155	101		104		88
280	53		53		59
Subject JV					
130	117	108	79	110	99
181	59	65	28	48	53
267	65	106	32	40	49

Response Latency for Right Location	Attention Allocation Condition				
	100	75	50	25	0
142	52	45	40	47	54
185	57	80	80	85	71
220	89	104	64	87	66
350	53	77	61	51	50
170	110		98		92
245	124		103		86
115	97	58	76	65	97
181	114	107	59	84	86
250	93	74	52	58	65

Table 4

Weighted amplitudes (fT) of neuromagnetic responses across attention allocation conditions

Second Task Set (Complex Discrimination)

Response Latency for Left Location	Attention Allocation Condition				
	100	75	50	25	0
Subject BR					
135	83	36	44	62	43
175	174	172	169	159	146
236	194	192	179	158	95
285	76	103	92	82	1 *
335	70	114	130	104	64
Subject SS					
130	94	79	53	70	72
250	74	57	46	87	39

Response Latency for Right Location	Attention Allocation Condition				
	100	75	50	25	0
Subject BR					
135	96	68	79	37	57
175	140	125	132	139	118
220	140	90	108	97	113
Subject SS					
115	84	48	74	61	68
160					
230	148	130	86	87	71

Relationships Between Physiology and Perception

We have considered how the functional aspects of neural activity in auditory cortex revealed by magnetic studies may relate to human perception or performance. The possibility of establishing such relationships is based on earlier studies of activity in visual cortex, where research in our laboratory showed that simple reaction time varies with stimulus parameters in the same way as the neuromagnetic latency for observing maximum field strength. This correspondence was established for the latency of steady-state responses to contrast-reversing grating patterns, where latency was found to increase with (1) increasing spatial frequency (Williamson et al. 1978), (2) decreasing contrast (Okada et al. 1982b) and (3) decreasing luminance (Okada et al., unpublished). We investigated a different aspect of neural activity in auditory cortex, taking advantage of the fact that neuromagnetic theory shows how quantitative measures of neural activity may be determined, both in

source strengths and source position in three-dimensional space. Our earlier studies of auditory responses combined with recent findings in other laboratories is a fertile basis for developing such relationships.

In 1982 studies by Romani et al. (1982a,b) demonstrated the existence of at least one tone map across human auditory cortex. The stimulus was a tone whose amplitude was sine-wave modulated at nearly 100%, and the magnetic response at the modulation frequency was mapped over the temporal and parietal areas of the head. Measurements of the total strength of the equivalent current dipole accounting for the observed field pattern showed that source strength is independent of tone frequency for a given subject. Also, for two subjects studied, strength was also independent of subject. This implies that the same number of neurons repond to a suprathreshold stimulus, regardless of frequency. The spatial extent of such a population cannot be inferred from the data (Okada, 1985), unless it were spread across cortex by a distance that exceeds the distance to the sensor, i.e., a distance of several centimeters.

Pantew et al. (1988) subsequently reported neuromagnetic evidence for a tonotopic sequence for the N100m component of the transient response to a tone burst. The general locus of activity agrees quite well with the trend observed in the steady-state response, with responses to tones of higher frequency lying deeper beneath the scalp. Thus both the N100m and steady-state response (the latter having an apparent latency of about 50 ms) are tonotopically organized. There is evidence these maps do not coincide, for careful measurements in our laboratory by Pelizzone et al. (1984) for the magnetic field patterns of N100m and steady-state response evoked by 1 kHz tones show that the two sources lie at the same depth but the steady-state response lies 1 cm more posterior than the transient.

Hoke et al. (1988) have also recently reported evidence for an amplitopic map for the N100m component, and the trajectory of this sequence across cortex is approximately at right angles to that of the tonotopic sequence, with activity shifting toward shallower depth and anteriorly with increasing stimulus intensity. Here as well as for the tonotopic sequence, there is a logarithmic representation, with cumulative distance across the cortex between one region of activity to another being proportional to the logarithm of the sound intensity. Each 10 dB increase in sound intensity produces a shift of about 0.3 cm across cortex.

The tonotopic and amplitopic functional maps have an interesting relationship to psychophysical studies of perception, and the two measures taken together provide an important physiological implication. To see this consider the fact that the just-noticeable tone difference for pitch discrimination at low levels of intensity is roughly proportional to frequency. This holds for frequencies down to about 1 kHz for studies with frequency-modulated tones (Shower and Biddulph, 1931) and down to about 500 Hz for successively presented tone bursts (Wier et al., 1977). These and other psychophysical data are discussed by Scharf and Buus (1986). The just-noticeable tone difference at a frequency f for tone bursts corresponds to a frequency shift of about $1 \times 10^{-3} f$. The tonotopic map reported by Romani et al. (1982b) indicates that a relative frequency shift of $\Delta f/f$ corresponds to displacement of activity across cortex by $\Delta D = 0.58(\Delta f/f)$ cm. Therefore the just-noticeable tone difference at low sound intensities represents a fixed shift of activity across cortex of about 6 μu. This is a remarkably short distance. It is much less than typical 'minicolumn' of Montcastle (1979), which is about 50 μu in diameter as determined by Nissl stain, and is even much less than the size of a single pyramidal cell, as gauged by the extent of dendritic arborization.

How much cortex is involved in producing a sensory evoked response in the MEG and EEG? This question was recently addressed in our laboratory by Lü and Williamson by analyzing published current source-density measurements. The measurements were obtained by inserting an array of electrodes through an appropriate area of sensory cortex and monitoring the voltage appearing at various depths as the brain responds to stimuli. Data for cat visual cortex and monkey somatosensory cortex were analyzed. The transcortical extracellular current at each depth was obtained by computing the first derivative with respect to depth of the potential profile. The second derivative with respect to depth indicates where current emerges from the intracellular space into the extracellular space ("current source-density") and where it re-enters the intracellular space. A measure of the quality of the data is obtained by determining how well the total emerging current matches the total disappearing current. By integrating this current source-density across cortex we obtain the transcortical current density. By integrating across cortex again we obtain the current dipole moment per millimeter of cortical area.

Most remarkably, for a wide range of stimuli, in both cat and monkey, the current dipole moment per square millimeter at moments of peak strength is nearly the same, for long latency components. The value we obtain is 50 picoampere-meter per square millimeter (50 pA·m/mm^2), with a variability of about a factor of 2 above and below this value. There are good reasons that this value may be applied to human cortex as well. Except for visual area 17 in primates, Rockel et al. (1980) report that there is a basic uniformity in cortical cell density across species. Their conclusion was based on observations for a variety of species that about 110 neurons are found in a 30-μm-width by 14-μm-length strip of cortex, from either motor, somatosensory, primary visual, frontal, parietal, or temporal areas. About 75% of these cells are pyramidal cells. The only exception to this common neuron count occurred in the binocular region of area 17 in primates, where about 2.5 times more neurons were found than in other areas. Therefore, it is reasonable to assume that the corresponding intracortical neuronal circuitry is similar across species. Since the total current dipole moment of sensory evoked responses obtained in neuromagnetic studies on humans lies within the range 2 – 20 nAm, we may infer that the corresponding cortical area extends over 40 – 400 mm^2. This result has been accepted for publication in *Experimental Brain Research* (Lü and Williamson, 1990).

Because the linear dimensions correxponding to such an area greatly exceed the shifts in the center of activity that correspond to the jnd for tone, a perceptually different tone is not distinguished by a discrete shift of all activity from one region of cortex to another (perhaps adjacent) one, as would be the case were it to shift from, say, one minicolumn to another. Instead the distance by which activity shifts is much smaller than the linear extent of the responding population. If tone discrimination is associated with activity giving rise to either the P50m or N100m transient components, the process may well depend on small shift in the position of the maximum of activity that is distributed along the cortex. It seems unlikely that the physiological processes underlying pitch discrimination are to be found at subcortical auditory nuclei, where tonotopic maps are also found, because these maps show more convergence (shorter total length of the tonotopic sequence) than at cochlea or cortex (Clopton et al. 1974).

The fact that very small displacements of activity across cortex may correspond to perceptual differences has been revealed previously in electrophysiological studies of activity in auditory cortex of the mustached bat, *Pteronotus parnellii parnellii*. Suga and Horikawa (1986) found that the just-noticeable range difference for determining the distance of a target at mid-range is about 1.3 cm, and this corresponds to a shift across cortex

of about 6 μm. Thus, fine-grain sensitivity is found for a variety of function sequences, in both primates and non-primates.

We may also consider psychophysical implications of the other dimension across auditory cortex - the amplitopic map. Our analysis of the data of Pantew et al. (1988) indicates that there is a shift of approximately 0.3 cm across cortex for each 10 dB increase in sound intensity. For a small relative change $\Delta I/I$ of intensity the corresponding displacement would be: $\Delta D = 0.13\ \Delta I/I$ cm. The data of Rabinowitz et al. (1976) and Jesteadt, Wier, and Green (1977) for just-noticeable differences in intensity show that discrimination improves with increasing intensity, from $\Delta I/I = 12 \times 10^{-2}$ at a sensation level of 40 dB to 5×10^{-2} at a sensation level of 80 dB. Accepting for the sake of illustration an intermediate value of 7×10^{-2} leads to the conclusion that the just-noticeable difference in sound level corresponds to a displacement of activity across cortex of about 100 μu. This is considerably greater than the minimium displacement along the tonotopic sequence corresponding to the just-noticeable tone difference. Yet it is much smaller than the characteristic dimension of several millimeters that we infer from the size of the cortical area that is activated. While this minimum required shift along the amplitopic sequence needed to account for the just-noticeable loudness difference is sufficiently large as to admit the notion that activity is displaced from one set of minicolumns to another, we would find this interpretation unlikely, for the extent of cortical activity in the orthogonal direction would have to be several centimeters. Therefore, it is more likely that the shift of activity across cortex for a jnd to tone or loudness is much less than the extent of activity along both those axes. The responding area of cortex to tones of just distinguishable pitch or loudness are largely overlapping.

Technical Developments

In addition to the experimental work summarized above, a number of technical tasks were accomplished over the course of the program. The most salient of these are described in this section of this final report.

Improved Dewar Gantry

To determine where neural sources lie within the head it is necessary to measure accurately the position and orientation of each field sensor with respect to landmarks on the subject's scalp. Traditionally the dewar containing the sensor was placed in the desired location, and the position of its tail with respect to convenient landmarks was measured across the scalp. But this procedure has inherent inaccuracies, due principally to the irregular shape of the head. One advance was to align the patient's head within a reference framework, and to move the dewar accurately with respect to this framework. The "Scanner" deviced developed in our laboratory (Williamson et al. 1984) is an example of such a setup where the dewar is held in a carriage that moves so that the dewar's axis always points toward the center of the patient's head. This has an advantage when the head is modeled as a sphere for computing source locations, for the field component provided by the sensors is exactly the radial component. Another procedure is to use a computer-controlled mechanized gantry that moves the dewar to a pre-determined position and orientation in space (Vrba et al. 1984). Recently we installed a commercial device for purposes of evaluation. Provided that the device performs properly, we shall make an effort to obtain funds to purchase it, so that it may remain in our laboratory.

The new gantry is based on a different principle which permits the operator to move the dewar by hand to the desired location. Independent movement is provided along two orthogonal horizontal directions and the vertical direction, with rotation allowed about the vertical axis and the horizontal axis where the gantry supports the dewar. Friction holds the dewar in place when the operator releases it, and a secure lock is provided by compressed gas brakes that secure all these degrees of freedom. The dewar can also be rotated about its own axis to set orientation of the individual sensors at a desired angle. The exact position and orientation of the dewar relative to the subject's head is indicated by a system known as the "Probe Position Indicator", purchased with funds from a DOD-University Research Initiative awarded by AFOSR.

"Rainbow" - A Device for Quantifying Positions in a Magnetic Resonance Image

The positions of field measurements about a subject's head are indicated in a coordinate system that we call the "head-based coordinates." It is defined with respect to the periauricular points and nasion, which are also the reference positions on which the EEG 10-20 electrode system is also based. One ultimate goal of the neuromagnetism program in our laboratory is to establish a three-dimensional functional image of the brain, in which regions of neural activity are shown in relationship to anatomical features. As a first step in this direction, we developed a system to define the same head-based coordinate system for magnetic resonance images (MRIs). A plexiglass framework called "Rainbow" was devised to embraces the subject's head when the MRI is recorded. Features on Rainbow are rendered as a series of bright spots on the MRI, so that by use of a 3D digitizer (such as the Probe Position Indicator) any position on the MRI can be related quantitatively to the head-based coordinate system.

Thus by digitizing one MRI slice after another, a 3D rendition of the subject's head can - in principle - be developed. In the future such a display could be shown on a solids rendering system such as the Hewlett Packard Model 9000/350SRX workstation. For the moment, graphics facilities in our laboratory can display an MRI slice in high resolution, with data transmitted from the MRI suite at University Hospital via NYU-NET. In addition, any 2D slice to be illustrated in line drawing format.

One application of 3D images will be to compare the orientation of the equivalent current dipole model representing neural activity with the local cortical topology. In this way it will be possible to determine whether the current lies perpendicular to the cortical surface or parallel. It would be the former if pyramidal cells or dendrites of other cells having preferred vertical orientations are responsible for the field, and the latter if directed projections from one area of cortex to another are responsible. Thus, important information concerning the underlying physiology can be deduced. Algorithms for digitizing the MRI scans and exploiting information provided by Rainbow have been developed by Ms. Gladys Klemic, a graduate student.

"Profile"- Software to Depict a Current Dipole in the Head

A graphics program christened "Profile" has been developed by Mr. Lian Tao, a graduate student, to relate the locations of deduced neural activity in the brain to external features of a subject's head. Profile displays on a terminal screen, or plots on an X-Y digital recorder, the three orthogonal profiles of a subject's head. The data are obtained by use of a 3D digitizer or the Probe Position Indicator system. The user chooses the side of the head to be displayed in the sagittal cross section, as well as whether the transverse cross section is to be depicted from below or above, and whether the coronal cross section is

seen from in front or in back. On each cross-section is shown the position and orientation of the dipole (or dipoles) that are deduced from field measurements to account for a measured field pattern. A vector depicts the dipole, and its length denotes the current dipole moment. A rectangle centered on the position indicates the uncertainty in the location of the dipole. The sagittal profile can also be distorted slightly to insure that the subject cannot be identified.

Method for Locating a Small Magnetic Object

During the course of this program we were presented with an opportunity to investigate the feasibility of using SQUID systems to locate a small magnetic object within the human body. While such an object would be modeled as a magnetic dipole, not a current dipole, we concluded that similar techniques could be applied in mapping the field pattern and using them to deduce where the object lies. Success in using such a procedure for a magnetic dipole would give additional confidence for using analogous procedures of localization for current dipoles. Furthermore, having a technology for detecting objects too small to be imaged by x-rays may have a variety of important applications.

The object of interest was a piece of a thin acupuncture needle lodged under the right scapula of a young male adult. It was estimated to be about 5 mm in length and only 0.2 mm in diameter. The needle could not be found in surgical procedures accompanied by studies of 30 standard X-ray images. To locate it, we mapped the magnetic field component normal to a plane lying above the object, using a standard SQUID neuromagnetometer. Assuming that the needle could be modelled as a magnetic dipole, we were able to infer its lateral position, depth, orientation, and magnetic moment. With this information, directed CT scans, high-resolution X-ray films, and the subsequent surgical removal of the needle proved that it could be located in the body with an accuracy of better than three millimeters. The principle limit on this accuracy is in specifying the location of the object relative to reference positions on the overlying skin. In this instance, different placements of the patient's right arm caused the skin to be displaced relative to the rib cage. Therefore, to achieve accurate localization the patient had to assume a given position for both the neuromagnetic studies and surgical procedure. This work was done in collaboration with Risto J. Ilmoniemi, Ph.D., Harold Weinberg, M.D., and Arthur D. Boyd, M.D.

To map the magnetic field pattern over the back, our patient lay prone on a firm bed, which was supported by rollers. During a scan, the bed was smoothly moved under the magnetometer, while its position was monitored by the voltage from a linear potentiometer attached to the bed. Each linear scan was performed three or more times to assure reliability; upon completion of a set of scans, the bed was displaced laterally by 2 cm and another set of scans was recorded. A pointer mounted on the dewar holder enabled us to reference positions across the plane of measurement to positions on the posterior torso. The only significant source of noise was a slow variation of the ambient field, which produces a drift of the baseline. The first depended upon identifying the positions of the positive and negative field extrema, as well as determining the values of the field at these extrema. We developed a procedure whereby this information is sufficient to determine the three position coordinates of the dipole, the two angles specifying its orientation, and the moment specifying its strength. We developed a set of curves that enables these parameters to be determined without recourse to a computer. A second method was based on using a computer routine to determine the least-squares fit to the field pattern. The deduced positions of the dipole determined by the two methods agreed to better than 3 mm, with the least-squares method being the more accurate because it more effectively averages over

imprecisions in the data.

Several verification tests were carried out with a 15-mm length of an acupuncture needle mounted on the subject bed, so that its position and orientation could be directly measured, confirmed the accuracy of this analysis. In fact, it was found that instrumental noise caused an error of only 0.8 mm in position. The position indicated by the magnetic analysis was used to determine where CT scans should be made, in an attempt to confirm the presence of the needle. Transverse scans through the thorax were obtained through the predicted location at 3-mm displacements longitudinally. A small (1-2 picture elements) high-density feature was evident in a single scan within the intercostal space between the fifth and sixth ribs, at the predicted depth and lateral position. Based on this information, a surgical procedure was scheduled. On the morning of the procedure, magnetic scanning was repeated with the subject prone and right arm raised above the head, mimicing the position to be assumed during surgery so that the deduced position could most accurately be related to marks placed on the skin. Subsequently, a high-resolution X-ray film was obtained for a frontal cross section of the upper right thorax, and it showed the needle curved at the lateral position indicated by the magnetic analysis. CT scans taken through and near the magnetically deduced position again confirmed the presence of the needle at the predicted depth. A surgical procedure was conducted with the incision made directly above the position indicated by the magnetic and X-ray studies. As soon as the depth of the incision was about 25 mm, the needle was observed in a curved configuration within the intercostal space between the fifth and sixth ribs, and it was removed. A paper describing this study has appeared in the IEEE Transactions of Biomedical Engineering (Ilmoniemi et al. 1988).

A New Method for Calibrating Multisensor SQUID Systems

Increasing interest in determining the strength of neural sources as well as their positions in the shortest possible time has drawn attention to the need for fixed arrays of sensors and for a method to accurately calibrate the individual sensors. Very accurate calibration is not of prime interest when an array is moved from one place to another sequentially to determine a field pattern, because generally the array is rotated from one measurement to the next in a quasi-random manner so that the effect of calibration inaccuracies tends to average toward zero. However, high accuracy becomes important when the array monitors the field pattern at a set of fixed positions over the scalp. We have developed a technique with a relative accuracy of about 2% for calibrating individual sensors in a neuromagnetic probe, whose detection coils have the popular geometry of a second-order gradiometer. This procedure was described in a paper that appeared in the IEEE Transactions of Biomedical Engineering (Costa Ribeiro et al. 1988).

It is quite simple to place a small calibration coil under the dewar, feed an ac current through its windings, and move the coil so that the sensor's output is maximized, thereby indicating the coil is centered on the axis of a given detection coil. However, the magnitude of the sensor's output is very sensitive to the distance between the calibration coil and detection coil, and this distance in general is not known to within the required fraction of a millimeter to achieve 1% accuracy. In practice the result has an accuracy of perhaps only 10%. A variation of this procedure relies on placing the coil in succession at a number of precisely determined locations sufficiently far from the probe that the field of the coil at the sensors is accurately dipolar. From the recorded outputs of all sensors for each coil location, high accuracy may be obtained when the calibration factors are determined by a least-squares fit (Ilmoniemi et al. 1988).

We have successfully applied another method for calibrating second-order gradiometers that relies precisely on the fact that such coils are relatively insensitive to a uniform field. The procedure is to use a large, square field coil whose sides (2.64 m length) are roughly two orders of magnitude greater than the baseline of the detection coil. A large *calibration coil* is placed so that the detection An ac current at 20 Hz is provided by a function generator, and the corresponding output of the SQUID electronics was amplified, bandpass filtered, and monitored by a digital voltmeter. This output is proportional to the difference between the field at the center coil and end coil of the detection coil, a number that is easily calculable from the known dimensions of the calibration coil and detection coil. Of particular importance is the fact that the net flux in the detection coil is insensitive to its exact position with respect to the calibration coil: moving one upward or downward by 4 cm produces only a 1% change in the value of the calibration factor. This is the desired feature of the large-coil technique.

The calibration factor determined in this way is accurate only to the extent that the detection coil's field balance (match of the area-turns ratio of all the coils of the gradiometer) is sufficiently high. The field imbalance can be determined by applying a uniform field and measuring the resulting output voltage of the sensor. For this purpose, a reasonably uniform field can be produced with a set of four coaxial, square coils of side 2.64 m (Merritt et al. 1983). The number of turns of wire in the four coils was originally 59,25,25,59. These field coils were positioned with an accuracy of better than 2 mm in an attempt to achieve sufficient field uniformity. Precise measurements of the resulting axial field profile (in the vertical direction) were made by differential methods with a fluxgate magnetometer to verify the quality of uniformity. They showed that the steel reinforcing rods in the concrete floor of the laboratory enhanced the field produced by the lowest coil and shifted the field center upwards from the geometrical center of the coil set. This effect could be countered by removing two turns of wire from the lowest coil.

To measure the effect of field imbalance in the windings of the detection coil, a 20-Hz current was passed through the uniform-field coil, and the corresponding ac output voltage of each SQUID system was noted with a digital voltmeter. Correcting for the small (about 3.5%) nonuniformity of the field yielded the field imbalance factor for each detection coil, which was on the order of 10^{-5}. Taking this into account for the measurements with the calibration coil yielded the calibration factor for the sensor. This is typically about 1.2×10^{-7} tesla/volt for the sensors in our 5-sensor probe (Freddy). The value of the calibration factor for each coil could be determined reproducibly with an accuracy of 2%. In comparing calibration factors across coils we found a 10% spread in their values, which may be attributed to differences in the construction of the SQUID systems.

A Method of Verification

Another way to measure the field imbalance correction, which at the same time verifies the value for the field calibration factor, is to measure the change in the output when the calibration coil is moved axially up or down by a known distance. If the displacement is small it is enough to consider the field profile only up to the fourth-order term. When displacing the calibration coil in our system by 4 cm the output voltage changes by only 1%, in agreement with the theory.

Single-Position Calibration

Another advantage of using a single large external coil for calibration is the possibility of doing it rapidly for all the sensors in an array. In fact it is not necessary to place each detection coil at the center and coaxially aligned with the calibration coil. The field produced by a large square calibration coil can be computed for the position of each turn of each detection coil. The theory for this was developed. Although this calibration procedure is comparatively insensitive to the vertical position of the calibration coil, it is nevertheless sensitive to other parameters such as the size of that coil: a 1% change in the length of the sides of the calibration coil affects the calibration by 3%. On the other hand, an error in the angular orientation by 1 deg affects the calibration by only 0.16%. Another advantage of this single-position calibration, beyond its rapidity, is the possibility of using it to determine the exact angular position of the array relative to a fixed laboratory frame of reference (the calibration coil) during an experiment where the array is tipped in order to be positioned over the source. The calibration factors can be determined prior to such a measurement, with the array upright, by passing a known current through the calibration coil.

Sources of Error in Determining the Location of a Neural Source

The early success of neuromagnetism motivated the development of magnetic sensing systems to measure the magnetic field near the scalp at several positions simultaneously. Probes with 4, 5, and 7 sensors are presently in use (Ilmoniemi 1984; Williamson et al. 1984; Romani 1985). In addition to greatly reducing the time required to record a field pattern, these multi-sensor systems make it possible to determine the position, strength, and orientation of a localized neural current source with a *single-position measurement*, that is, without having to move the probe from one place to another. A particular advantage of this is the possibility of following subtle shifts of activity between adjacent neural populations in studies such as those recording responses evoked by visual patterns of differing content.

The effects of calibration error and magnetic noise on the accuracy of locating an equivalent current dipole source in the human brain were investigated by computer analysis for 5- and 7-sensor probes and for a pair of 7-sensor probes. The importance of using a large array, with sensors strategically placed, is illustrated by an analysis for case when the probe is placed at a field extremum. Then a noise level of 5% of peak detected signal produced uncertainties of about 20% in source strength and depth for a 5-sensor probe. These are reduced to 8% when the array is increased to a pair of 7-sensor probes, and uncertainties of about 15 mm in lateral position with the 5-sensor probe are reduced to 1 mm for the pair of 7-sensor probes.

The head was modeled as a uniform sphere or a set of concentric spherical shells of differing conductivity, representing regions such as the brain, skull, and dermis. The source was modeled as a current dipole, which is described by five parameters: its position (x, y, z), orientation ψ of its moment in the plane tangential to the radius passing through its location, and the value Q of this moment. The five field values obtained from a single-position measurement with a 5-sensor probe are sufficient to determine these five parameters, provided that the probe is not centered on certain symmetry lines or points, such as directly over the dipole (Hämäläinen et al. 1985; Ilmoniemi 1985). Indeed, if additional information is available to fix the orientation of the source, a four-sensor system may serve for locating a dipole (Vyedensky et al. 1988). However, we might expect that locating a dipole with a 4- or 5-sensor system is very sensitive to calibration errors since the

parameters are not overdetermined by the data. The computations were made for successively larger arrays of sensors presently in use: a 5-sensor probe with 4 outer coils equally spaced about a central coil; a 7-sensor probe with 6 outer coils equally spaced about a central coil; and a pair of 7-sensor probes (hereafter called a 14-sensor system). The probe in these computations was placed directly over a position on the scalp where the normal component of the field is maximum, which is useful for achieving good accuracy in determining the depth and strength of a current dipole. The five-sensor probe we considered has a set of five detection coils (Freddy), each being a second-order gradiometer with a coil radius $a = 0.75$ cm and baseline $b = 4.0$ cm between adjacent coils. The coils are arranged in the pattern of a cross, so that the centers of the pickup coils (lowest coil of the gradiometer) of the four outer coils are 2.0 cm from the axis of symmetry. The seven-sensor probe is identical to the 5-sensor probe except that it has two additional outer sensors, thus forming a hexagonal array about the center coil. The fourteen-sensor probe consists of two 7-sensor probes, positioned at each field extremum with identical orientations.

Effect of Calibration Errors

Certain detection coil positions play more important roles than others in determining the values of various dipole parameters obtained from a least-squares fit to the data. To illustrate this we computed the consequence of a calibration error in any one of the sensors. Nonlinearity in the relationship between field values and best-fitting parameters was evident, because identical positive and negative increments generally changed each parameter in opposite directions but by different amounts. We took the larger change to characterize the corresponding uncertainty in the best-fitting value. Our computations show that an error as small as 1% in *any* sensor causes the dipole to rotate and shift by ~5 mm in the coordinate z longitudinal to the direction of the dipole. If the errant sensor lies off the axis passing through the extrema of the field pattern, the shift is due to breaking of mirror symmetry about this line.

The lateral position x is influenced most strongly by errors in the center sensor and the one farthest from the dipole. The center field in comparison with fields at the outer sensors fixes the depth of the dipole and therefore how far it lies from the probe. Longitudainal position z is also influenced more strongly by coils lying farther from the dipole. The orientation ψ of the dipole's moment is related to this, being most sensitive to error in the farthest sensor, with all of the others being much less important. The deduced depth d of the dipole is most sensitive to a calibration error for the center sensor. This is because its signal in comparison with those of the outer sensors determines the scale length of the pattern: a stronger signal decreases the length scale, thus implying a shallower dipole, and *vice versa*. The strength Q of the dipole is also most sensitive to the field indicated by the center sensor. While Q is directly related to the field at the extremum it is also affected by the depth of the dipole: to produce a given maximum field, the deduced Q must increase with increasing depth.

Similar computations have been carried out for 7-sensor and 14-sensor probes. The effects of calibration errors for the center sensor, sensors nearest the dipole, or sensors farthest from the dipole are similar, but the magnitude of the maximum shift of a dipole parameter is generally reduced. Part of this advantage comes from the effect of diluting the importance of any one sensor when the total number of sensors is increased, and in the case of the 14-sensor probe part comes from the broader expanse of the field pattern that is sampled. One exception to the improvement in accuracy with increasing number of sensors is determination of the parameters Q and d with the 5-sensor and 7-sensor probes. This is

because the center sensor has dominant importance for these parameters in comparison with any of the outer sensors, so a calibration error for the center sensor produces virtually the same change in Q and d for both the 5-sensor and 7-sensor probes. To emphasize this point, there is a dramatic improvement in the precision for Q and d when the second 7-sensor probe is positioned over the other field extremum to produce a 14-sensor system. Determining the locations of the two extrema fixes the length scale of the pattern more firmly than the ratio of central to outer fields of any one extrema, thus reducing the importance of both center sensors.

In view of these trends, we conclude that the scalar properties (strength Q and depth d) have values that are most sensitive to calibration errors in the central sensor, whereas the vector properties (longitudinal and transverse position, as well as orientation) are most sensitive to the coils placed farthest from the source. We emphasize that these trends apply when the probes are placed directly over the field extrema, so as to monitor the strongest fields. There is no implication in this choice of position that it is optimal for determining the full set of dipole parameters; indeed, the optimal position and orientation of the probe will depend on the parameter of interest and on the depth of the dipole.

Influence of Noise on Locating a Source

The preceding discussion of calibration errors has a straightforward extension to the effect of field noise on the uncertainty in the best-fitting values of the dipole parameters. For simplicity we assume that the noise in the various sensors is uncorrelated and of the same rms value. To generalize the discussion, it is convenient to express the rms field noise in any sensor in terms of the field at the positive extremum. Thus, when the same normalized noise amplitude is applied to an outer coil, which has a lower signal level, the actual signal-to-noise ratio for that coil is worse than for the center coil. The results for the 5-sensor, 7-sensor, and 14-sensor probes are shown in Table I. On going from 5 to 7 sensors, there is substantial improvement in reducing the uncertainties for some parameters (x, z, ψ), while there is very little benefit for others (Q and d). The most dramatic improvement is obtained on going from the 7-sensor to 14-sensor probe, where all the uncertainties are diminished. The reason is evident: On going from 5 to 7 sensors the additional outer detection coils enhance the probe's ability to resolve asymmetry in the field pattern, and this better establishes the position (x,z) and orientation ψ of the source with respect to a field extremum. A similar improvement is seen on going from 7 sensors to 14 sensors, but there is also a marked improvement in determining Q and d. The latter benefit was gained because placing a second probe over the second field extremum accurately fixes the distance between the extrema of the pattern, thereby more accurately determining d. Then the average of the field values accurately fixes Q. In addition, determining the general location of both extrema limits the uncertainty in the dipole's orientation ψ. This was said in a different way by Ahonen et al. (1986) who noted that the accuracy of a dipole fit is enhanced for an array of sensors if the lateral spacing between their detection coils is increased, even if the dipole lies at a relatively shallow depth. Cuffin (1986) has also considered the effect of noise on dipole localization for several types of measurements, and although the position of the probe in his calculations does not coincide with ours there is general agreement between his results and ours for the uncertainty in strength, orientation, and depth of the dipole source.

It may be concluded that the 5-sensor probe with a 10% noise level produces rather poor results: the source strength is known to only about 40%, its orientation to only 60°, and the lateral position to only 2 cm. Decreasing the noise to 5% provides substantial

Table 5

Magnitude of the uncertainties in best-fitting current-dipole parameters for various levels of field noise in the sensors. Noise is expressed as a percentage of the dipole's field at a field extremum. The dipole is located at a depth of 2 cm beneath the surface of a uniform conducting sphere of radius 9 cm.

PROBE (%)	NOISE (%)	$\delta Q/Q$ (%)	$\delta d/d$ (%)	δx (mm)	δz (mm)	$\delta \psi$ (deg)
5-sensor	5	21	16	4.6	13.6	40
	10	42	31	6.7	20.0	64
7-sensor	5	20	15	1.2	4.0	12
	10	44	31	2.6	8.1	14
14-sensor	5	8	6	0.4	1.0	3
	10	16	11	0.8	1.9	6

improvements, with uncertainties that are comparable to much of the data being reported in the literature with a single sensor being used for sequential measurements at some 30 or more positions.

The main advantage in adding two more sensors to produce a 7-sensor probe is in improving the uncertainty in position and orientation of the dipole. For a comparable noise level, these uncertainties are reduced by a factor of 2 - 3. A further reduction of ~3 is achieved in the uncertainties for *all* parameters by going to a 14-sensor probe. Here the results are comparable to what might be considered state-of-the-art, where Q and d are known to about 10%, transverse position to 1-2 mm, and orientation to 10°. Clearly, a 5% noise level with a 14-sensor probe would represent a substantial advance on this. High precision of this type is advantageous when searching for subtle changes in position or orientation of a confined neural population under study. These small uncertainties are comparable to the practical limits imposed by variability of many types of biomagnetic activity and by errors attendant to positioning a probe over the scalp.

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Personnel

The following personnel received partial support during the course of this URI program:

Lloyd Kaufman, Ph.D., Principal Investigator
Professor of Psychology and Neural Science

Samuel J. Williamson, Sc.D., Co-Principal Investigator
Professor of Physics and Neural Science
Professor of Physiology and Biophysics

Linda Davis-Ore, Administrative Secretary

Risto J. Ilmoniemi, Ph.D.
Research Scientist

Joan Gay Snodgrass, Ph. D.
Professor of Psychology

Jean Claude Falmagne, Ph. D.
Professor of Psychology

Sarah Curtis, Ph.D.
formerly, Graduate Research Assistant in Psychology
Research Scientist

Gladys Klemic
Graduate Research Assistant in Physics

James Shang
Graduate Research Assistant in Physics

Lian Tao
Graduate Research Assistant in Physics

David Travis, Ph.D. in Psychology
Postdoctoral Fellow

Bruce Luber
Graduate Research Assistant in Psychology

Mathew Koppen, Ph.D.
Postdoctoral Fellow

John Adams
Graduate Research Assistant in Psychology

Unsupported collaborators were:

Olli Lounassmaa, Ph.D.
Professor of the Finnish Academy of Science

Dr. Risto Ilmoniemi
Postdoctoral Scientist

Dr. Paolo Costa Rubeiro
Postdoctoral Scientist

John Krauskopf, Ph.D.
Research Professor of Neural Science

Murray Glanzer, Ph.D.
Professor of Psychology

George Sperling, Ph. D.
Professor of Psychology and Neural Science

Publications from the Neuromagnetism Laboratory

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